REFERENCES

1. Eisenbarth GS. Type I diabetes mellitus: A chronic autoimmune disease. N Engl J Med 1986; 314:1360-1368.
2. Falqui L, Martinenghi S, Severini GM, et al. Reversal of diabetes in mice by implantation of human fibroblasts genetically engineered to release mature human insulin. Human Gene Therapy 1999; 10:1753-1762.
3. Muzzin P, Eisensmith RC, Copeland KC, Woo SLC. Hepatic insulin gene expression as treatment for Type 1 diabetes mellitus in rats. Mol Endo 1997; 11:833-837.
4. Gros L, Riu E, Montoliu L, Ontiveros M, Lebrigand L, Bosch F. Insulin production by engineered muscle cells. Human Gene Therapy 1999; 10:1207-1217.
5. Short DK, Okada S, Yamauchi K, Pessin JE. Adenovirus-mediated transfer of a modified human proinsulin gene reverses hyperglycemia in diabetic mice. American Journal of Physiology 1998; 275:E748-E756.
6. Rivera VM, Wang W, Wardwell S, et al. Regulation of protein secretion through controlled aggregation in the endoplasmic reticulum. Science 2000; 287:826-830.
7. Selden RF, Skoskiewicz MJ, Russell PS, Goodman HM. Regulation of insulin-gene expression. N Engl J Med 1987; 317:1067-1076.
8. Kolodka TM, Finegold M, Moss L, Woo SLC. Gene therapy for diabetes mellitus in rats by hepatic expression of insulin. Proc Natl Acad Sci USA 1995; 92:3293-3297.
9. Tuch BE, Tabiin MT, Casamento FM, Simpson AM, Marshall GM. Transplantation of genetically engineered insulin-producing hepatocytes

into immunoincompetent mice. Transplantation Proceedings 1998; 30:473.

10. Valera A, Fillat C, Costa C, et al. Regulated expression of human insulin in the liver of transgenic mice corrects diabetic alterations. FASEB J 1994; 8:440-447.
11. Kaneda Y, Iwai K, Uchida T. Introduction and expression of the human insulin gene in adult rat liver. Journal of Biological Chemistry 1989; 264:12126-12129.
12. Yamaguchi M, Kuzume M, Matusumoto T, et al. Insulin gene transfer compensates pancreatic á-cell function in diabetic rats. Transplantation Proceedings 1998; 30:2913.
13. Sugiyama A, Hattori S, Tanaka S, et al. Defective adenoassociated viral-mediated transfection of insulin gene by direct injection into liver parenchyma decreases blood glucose of diabetic mice. Hormone and Metabolic Research 1997; 29:599-603.
14. Abai A, Hobart P, Barnhart KM. Insulin Delivery with Plasmid DNA. Human Gene Therapy 1999; 10:2637-2649.
15. Lu D, Tamemoto H, Shibata H, Saito I, Takeuchi T. Regulatable production of insulin from primary-cultured hepatocytes: insulin production is up-regulated by glucagon and cAMP and down-regulated by insulin. Gene Therapy 1998; 5:888-895.
16. Gros L, Montoliu L, Riu E, Lebrigand L, Bosch F. Regulated production of mature insulin by non-b-cells. Human Gene Therapy 1997; 8:2249-2259.
17. Wanke IE, Wong NC. Specific problems facing gene therapy for insulin-dependent diabetes mellitus: glucose-regulated insulin secretion from hepatocytes. Proceeding of the Western Pharmacology Society 1997; 40:131-133.

18. Simpson AM, Marshall GM, Tuch BE, et al. Gene therapy of diabetes: glucose-stimulated insulin secretion in a human hepatoma cell line (HEP G2ins/g). Gene Therapy 1997; 4:1202-1215.

19. Powell DR, Suwanichkul A, Cubbage M, Lee PDK. Regulation of insulin-like growth factor binding protein-1 (IGFBP-1) protein levels, mRNA levels and promoter activity by insulin (IN) and IGF-1 in HepG2. Endo Society 1990:280A.

20. Powell DR, Suwanichkul A, Cubbage ML, DePaolis LA, Snuggs MB, Lee PDK. Insulin inhibits transcription of the human gene for insulin-like growth factor-binding protein-1. Journal of Biological Chemistry 1991; 266:18868-18876.

21. Powell DR, Suwanichkul A. HNF1 activates transcription of the human gene for insulin-like growth factor binding protein-1. DNA and Cell Biology 1993; 12:283-289.

22. Suwanichkul A, Cubbage ML, Powell DR. The promoter of the human gene for insulin-like growth factor binding protein-1. Basal promoter activity in HEP G2 cells depends upon liver factor B1. Journal of Biological Chemistry 1990; 265:21185-21193.

23. Suwanichkul A, DePaolis LA, Lee PDK, Powell DR. Identification of a promoter element which participates in cAMP-stimulated expression of human insulin-like growth factor-binding protein-1. Journal of Biological Chemistry 1993; 268:9730-9736.

24. Suwanichkul A, Morris SL, Powell DR. Identification of an insulin-responsive element in the promoter of the human gene for insulin-like growth factor binding protein-1. Journal of Biological Chemistry 1993; 268:17063-17068.

25. Suwanichkul A, Allander SV, Morris SL, Powell DR. Glucocorticoids and insulin regulate expression of the human gene for insulin-like growth

factor-binding protein-1 through proximal promoter elements. Journal of Biological Chemistry 1994; 269:30835-30841.

26. Hughes SD, Johnson JH, Quaade C, Newgard CB. Engineering of glucose-stimulated insulin secretion and biosynthesis in non-islet cells. 1992; 89:688-692.

27. Rencurel F, Waever G, Antoine B, et al. Requirement of glucose metabolism for regulation of glucose transporter type 2 (GLUT 2) gene expression in liver. Biochemical Journal 1996; 314:903-909.

28. Villafuerte BC, Goldstein S, Murphy LJ, Phillips LS. Nutrition and Somatomedin XXV. Regulation of insulin-like growth factor binding protein-1 in primary cultures of normal rat hepatocytes. Diabetes 1991; 40:837-841.

29. Ooi GT, Tseng LY-H, Tran MQ, Rechler MM. Insulin rapidly decreases insulin-like growth factor-binding protein-1 gene transcription in streptozotocin-diabetic rats. Molecular Endocrinology 1992; 6:2219-2228.

30. Pao C-I, Farmer PK, Begovic S, Goldstein S, Wu G-J, Phillips LS. Expression of hepatic insulin-like growth factor-I and insulin-like growth factor-binding protein-1 genes is transcriptionally regulated in streptozotocin-diabetic rats. Molecular Endocrinology 1992; 6:969-977.

31. Suh D-S, Zhou Y, Ooi GT, Rechler MM. Dexamethasone stimulation of rat insulin-like growth factor binding protein-1 (IGFBP-1) promoter activity involves the interaction of multiple transcription factors. Progress in Growth Factor Research 1995; 6:131-140.

32. Cuif M-H, Cognet M, Boquet D, Tremp G, Kahn A, Vaulont S. Elements responsible for hormonal control and tissue specificity of L-type pyruvate kinase gene expression in transgenic mice. Molecular and Cellular Biology 1992; 12:4852-4861.

33. Cognet M, Lone YC, Vaulont S, Kahn A, Marie J. Structure of the rat L-type pyruvate kinase gene. J Mol Biol 1987; 196:11-25.

34. Bergot M-O, Diaz-Guerra M-JM, Puzenat N, Raymondjean M, Kahn A. Cis-regulation of the L-type pyruvate kinase gene promoter by glucose, insulin and cyclic AMP. Nucleic Acids Research 1992; 20:1871-1878.

35. Vaulont S, Munnich A, Decauz J-F, Kahn A. Transcriptional and post-transcriptional regulation of L-type pyruvate kianse gene expression in rat liver. Journal of Biological Chemistry 1986; 261:7621-7625.

36. Goswami R, Lacson R, Unterman T. Identification of insulin and glucocorticoid response sequences in the rat IGF binding protein-1 (IGFBP-1) promoter. Endocrine Society 1993; 1915B:529.

37. Shu D-S, Ooi GT, Lesniak MAS. Inhibition of IGFBP-1 gene expression by insulin and stimulation by dexamethasone, cyclic amp, and phorbol esters are mediated by different cis-acting elements in the rat IGFBP-1 promoter. Endocrine Society 1993; 1916B:529.

38. Bergot M-O, Diaz-Guerra M-JM, Puzenat N, Raymondjean M, Kahn A. Cis -regulation of the L-type pyruvate kinase gene promoter by glucose, insulin and cyclic AMP. Nucleic Acids Res 1992; 20:1871-1878.

39. Smeekens SP, Chan SJ, Steiner DF. The biosynthesis and processing of neuroendocrine peptides: identification of proprotein convertases involved in intravesicular processing. Progress in Brain Research 1992; 92:235-246.

40. Groskreutz DJ, Sliwkowski MX, Gorman CM. Genetically engineered proinsulin constitutively processed and secreted as mature, active insulin. Journal of Biological Chemistry 1994; 269:6241-6245.

41. Steiner DF, Smeekens SP, Ohagi S, Chan SJ. The New Enzymology of Precursor Processing Endoproteases. Journal of Biological Chemistry 1992; 267:23435-23438.

42. Simonson GD, Groskreutz DJ, Gorman CM, MacDonald MJ. Synthesis and processing of genetically modified human proinsulin by rat myoblast primary cultures. Human Gene Therapy 1996; 7:71-78.

43. Unger RH, Foster DW. Chapter 21. In: Wilson JD, Foster DW, Kronenberg HM, Williams RH, eds. Williams Textbook of Endocrinology. Vol. 9th. Philadelphia, London, Toronto, Montreal, Sydney: W.B Saunders Co., 1998:973-1059.

44. Robertson DG, Marino EM, Thule PM, Seneviratne CK, Murphy LJ. Insulin and glucocorticoids regulate IGFBP-1 expression via a common promoter region. Biochemical Biophysical Research Communication 1994; 200:226-232.

45. Goswami R, Lacson R, Yang E, Sam R, Unterman T. Functional analysis of glucocorticoid and insulin response sequences in the rat insulin-like growth factor-binding protein-1 promoter. Endocrinology 1994; 134:736-743.

46. Suh DS, Ooi GT, Rechler MM. Identification of cis -elements mediating the stimulation of rat insulin-like growth factor-binding protein-1 promoter activity by dexamethasone, cyclic adenosine 3',5'-monophosphate, and phorbol esters, and inhibition by insulin. Molecular Endocrinology 1994; 8:794-805.

47. Goldstein S, Sertich G, Levan KR, Phillips LS. Nutrition and somatomedin. XIX. Molecular regulation of insulin-like growth factor-I in streptozotocin-diabetic rats. Molecular Endocrinology 1988; 2:1093-1100.

48. Minematsu S, Watanabe M, Tsuchiya N, Amagaya S. Diurnal variations in blood chemical items in Sprague-Dawley rats. Experimental Animals 1995; 44:223-232.

49. Haughton CL, Dillehay DL, Phillips LS. Insulin replacement therapy for the rat model of streptozotocin-induced diabetes mellitus. Laboratory Animal Science 1999; 49:639-44.

50. Koopmans SJ, Sips HCM, Krans HMJ, Radder JK. Pulsatile intravenous insulin replacement in streptozotocin-diabetic rats is more efficient than continuous delivery:effects on glycaemic control, insulin-mediated glucose metabolism and lipolysis. Diabetologia 1996; 39:391-400.

51. Wang RN, Bouwens L, Kloeppel G. Beta-cell proliferation in normal and streptozotocin-treated newborn rats: site, dynamics and capacity. Diabetologia 1994; 37:1088-1096.

52. Like AA, Guberski DL, Butler L. Influence of Environmental Viral Agents on Frequency and Tempo of Diabetes Mellitus in BB/Wor Rats. Diabetes 1991; 40:259-262.

53. Seglen PO. Preparation of rat liver cells. III. Enzymatic requirements for tissue dispersion. Exp Cell Res 1973; 82:391-398.

54. Ginot F, Decaux J-F, Cognet M, et al. Transfection of hepatic genes into adult rat hepatocytes in primary culture and their tissue-specific expression. Eur J Biochem 1989; 180:289-294.

55. Baker A, Saltik M, Lehrmann H, et al. Polyethylenimine (PEI) is a simple, inexpensive and effective reagent for condensing and linking plasmid DNA to adenovirus for gene delivery. Gene Therapy 1997; 4:773-782.

56. Marriott D, Gillece-Castro B, Gorman CM. Prohormone convertase-1 will process prorelaxin, a member of the insulin family of hormones. Molecular Endocrinology 1992; 6:1441-1450.

57. Mittereder N, March KL, Trapnell BC. Evaluation of the concentration and bioactivity of adenovirus vectors for gene therapy. Journal of Virology 1996; 70:7498-7509.